

AMENDMENT

In the Specification:

Please enter the accompanying Sequence Listing into the application.

Please amend the paragraph beginning at page 1, line 2 as follows:

This application is a continuation application of US patent application no. 09/302,626, filed April 30, 1999, which is a continuation-in-part of international patent application PCT/IB99/00103, filed January 14, 1999, from which priority is claimed under 35 U.S.C. § 119 120, and claims priority under 35. U.S.C § 119 to Great Britain application nos. GB9800022143.5, filed on October 9, 1998, GB9819015.0, filed on September 1, 1998, and GB9800760.2, filed on January 14, 1998, which applications are incorporated herein by reference in their entireties.

Please amend the paragraph beginning on page 50, line 8 as follows:

Figures ~~1-7~~ 1A-E show biochemical data and sequence analysis pertaining to ~~Examples 1, 2, 3, 7, 13, 16 and 19, respectively, with ORFs 40, 38, 44, 52, 114, 41 and 124..~~ M1 and M2 are molecular weight markers. Arrows indicate the position of the main recombinant product or, in Western blots, the position of the main *N.meningitidis* immunoreactive band. TP indicates *N.meningitidis* total protein extract; OMV indicates *N.meningitidis* outer membrane vesicle preparation. In bactericidal assay results: a diamond (◆) shows preimmune data; a triangle (Δ) shows GST control data; a circle (●) shows data with recombinant *N.meningitidis* protein. Computer analyses show a hydrophilicity plot (upper), an antigenic index plot (middle), and an AMPHI analysis (lower). The AMPHI program has been used to predict T-cell epitopes [Gao *et al.* (1989) *J. Immunol.* 143:3007; Roberts *et al.* (1996) *AIDS Res Hum Retrovir* 12:593; Quakyi *et al.* (1992)

Scand J Immunol suppl.11:9) and is available in the Protean package of DNASTAR, Inc. (1228 South Park Street, Madison, Wisconsin 53715 USA). ORF 40. Figure 1A shows the results of affinity purification and Figure 1B shows the results of expression of the GST-fusion in *E. coli*, where M2 and M1 are molecular weight markers, and Arrows indicate the position of the main recombinant product. Figure 1C shows the results of FACS analysis of the sera of mice that were immunized with the purified protein. Figure 1D shows the results of bactericidal assay where a diamond (◆) shows preimmune data; a triangle (▲) shows GST control data; and a circle (●) shows data with recombinant *N. meningitidis* protein. Figure 1E shows computer analysis showing a hydrophilicity plot (upper), an antigenic index plot (middle), and an AMPHI analysis (lower). The AMPHI program has been used to predict T-cell epitopes (Gao *et al.* (1989) *J. Immunol.* 143:3007; Roberts *et al.* (1996) *AIDS Res Hum Retrovir* 12:593; Quakyi *et al.* (1992) *Scand J. Immunol* suppl. 11:9) and is available in the Protean Package of DNASTAR, Inc. (1228 South Park Street, Madison, Wisconsin 53715 USA).

Figures 2A-E show biochemical data and sequence analysis pertaining to ORF 38-1. Figure 2A shows the results of affinity purification and Figure 2B shows the results of expression of the GST-fusion in *E. coli*, where M2 and M1 are molecular weight markers, and Arrows indicate the position of the main recombinant product. Figure 2C shows the results of FACS analysis of the sera of mice that were immunized with the purified protein. Figure 2D shows the results of bactericidal assay where a diamond (◆) shows preimmune data; a triangle (▲) shows GST control data; and a circle (●) shows data with recombinant *N. meningitidis* protein. Figure 2E shows plots of hydrophilicity plot (upper), an antigenic index plot (middle), and an AMPHI analysis (lower).

Figures 3A-D show biochemical data and sequence analysis pertaining to ORF 44-1. Figure 3A shows the results of affinity purification and Figure 3B shows the results of expression of the GST-fusion in *E. coli*, where M2 and M1 are molecular weight

markers, and Arrows indicate the position of the main recombinant product. Figure 3C shows the results of bactericidal assay where a diamond (◆) shows preimmune data; a triangle (▲) shows GST control data; and a circle (●) shows data with recombinant *N. meningitidis* protein. Figure 3D shows plots of hydrophilicity plot (upper), an antigenic index plot (middle), and an AMPHI analysis (lower).

Figure 4A shows the results of affinity purification of ORF 52, where M1 is a molecular weight marker, and the arrow indicates the position of the main recombinant product. Figure 4B shows a hydrophilicity plot (upper), an antigenic index plot (middle), and an AMPHI analysis (lower).

Figure 5 shows a hydrophilicity plot (upper), an antigenic index plot (middle), and an AMPHI analysis (lower) for ORF 114.

Figure 6 shows a hydrophilicity plot (upper), an antigenic index plot (middle), and an AMPHI analysis (lower) for ORF 41.

Figure 7 shows a hydrophilicity plot (upper), an antigenic index plot (middle), and an AMPHI analysis (lower) for ORF 124.

Please amend the paragraph beginning on page 50, line 20 as follows:

Figure 8 shows an alignment comparison of amino acid sequences for ORF 40 for several strains of *Neisseria* (zn07 1, SEQ ID NO:96; zn20 1, SEQ ID NO:104; zn21 1, SEQ ID NO:105; zn06 1, SEQ ID NO:95; zn19 1, SEQ ID NO:103; zn03 1, SEQ ID NO:93; zn18 1, SEQ ID NO:102; zn11 ass, SEQ ID NO:99; zn02 1, SEQ ID NO:92; zn04 1, SEQ ID NO:94; zn16 1, SEQ ID NO:101; zn14 1, SEQ ID NO:100; z2491, SEQ ID NO:91; zn10 1, SEQ ID NO:98; zn22 1, SEQ ID NO:106; zn23 1, SEQ ID NO:107; zn28 ass, SEQ ID NO:110; zn24 1, SEQ ID NO:108; zn25 ass, SEQ ID NO:109; zn08 1, SEQ ID NO:97; zn29 ass, SEQ ID NO:111). Dark shading indicates regions of homology, and gray shading indicates the conservation of amino acids with

similar characteristics. The Figure demonstrates a high degree of conservation among the various strains, further confirming its utility as an antigen for both vaccines and diagnostics.

Please amend the paragraph beginning on page 53, line 15 as follows:

5'-end primer tail: <u>CGCGGATCCCATATG</u>	(<i>Bam</i> HI- <i>Nde</i> I)	(SEQ ID NO:134)
<u>CGCGGATCCGCTAGC</u>	(<i>Bam</i> HI- <i>Nhe</i> I)	(SEQ ID NO:135)
<u>CCGGAATTCTAGCTAGC</u>	(<i>Eco</i> RI- <i>Nhe</i> I)	(SEQ ID NO:136)
3'-end primer tail: <u>CCCGCTCGAG</u>	(<i>Xho</i> I)	(SEQ ID NO:137)

Please amend the paragraph beginning on page 67, line 10 as follows:

The originally-identified partial strain B sequence (ORF40 (SEQ ID NO:2)) shows 65.7% identity over a 254aa overlap with ORF40a (SEQ ID NO:138):

Please amend the paragraph beginning on page 67, line 42 as follows:

The complete strain B sequence (ORF40-1 (SEQ ID NO:4)) and ORF40a (SEQ ID NO:6) show 83.7% identity in 601 aa overlap:

Please amend the paragraph beginning on page 68, line 46 as follows:

ORF40 (SEQ ID NO:2) and Hsf protein (SEQ ID NO:139) show 54% aa identity (SEQ ID NO:140) in 251 aa overlap:

Please amend the section on page 69, lines 5 to 46 as follows:

gi|1666683 (U41852) hsf gene product [*Haemophilus influenzae*] Length = 2353
Score = 153 (67.7 bits), Expect = 1.5e-116, Sum P(11) = 1.5e-116

Identities = 33/36 (91%), Positives = 34/36 (94%)

Query: 16 VAVSELTRNHTKRASATVKTAVLATLLFATVQANAT 51 (SEQ ID NO:141)
V VSELTR HTKRASATV+TAVLATLLFATVQANAT (SEQ ID NO:142)
Sbjct: 17 VVSELTRTHTKRASATVETAVLATLLFATVQANAT 52 (SEQ ID NO:143)

Score = 161 (71.2 bits), Expect = 1.5e-116, Sum P(11) = 1.5e-116
Identities = 32/38 (84%), Positives = 36/38 (94%)

Query: 101 VTLKAGDNLKIKQNTNENTNASSFTYSLKKDLTG LINV 138 (SEQ ID NO:144)
+TLKAGDNLKIKQNT+E+TNASSFTYSLKKDLT L +V (SEQ ID NO:145)
Sbjct: 103 ITLKAGDNLKIKQNTDESTNASSFTYSLKKDLTDLTSV 140 (SEQ ID NO:146)

Score = 110 (48.7 bits), Expect = 1.5e-116, Sum P(11) = 1.5e-116
Identities = 21/29 (72%), Positives = 25/29 (86%)

Query: 138 VTEKLSFGANGKKVNIISDTKGLNFAKET 166 (SEQ ID NO:147)
V++KLS G NG KVNI SDTKGLNFAK++ (SEQ ID NO:148)
Sbjct: 1439 VSDKLSLGTNGNKVNITSDTKGLNFAKDS 1467 (SEQ ID NO:149)

Score = 85 (37.6 bits), Expect = 1.5e-116, Sum P(11) = 1.5e-116
Identities = 18/32 (56%), Positives = 20/32 (62%)

Query: 169 TNGDTTVHLNGIGSTLTDTLAGSSASHVDAGN 200 (SEQ ID NO:150)
T D +HLNGI STLTDTL S A+ GN (SEQ ID NO:151)
Sbjct: 1469 TGDDANIHLNGIASTLTDTLLNSGATTNLGNN 1500 (SEQ ID NO:152)

Score = 92 (40.7 bits), Expect = 1.5e-116, Sum P(11) = 1.5e-116
Identities = 16/19 (84%), Positives = 19/19 (100%)

Query: 206 RAASIKDVLNAGWNIKGVK 224 (SEQ ID NO:153)
RAAS+KDVLNAGWN++GVK (SEQ ID NO:154)
Sbjct: 1509 RAASVKDVLNAGWNVRGVK 1527 (SEQ ID NO:155)

Score = 90 (39.8 bits), Expect = 1.5e-116, Sum P(11) = 1.5e-116
Identities = 17/28 (60%), Positives = 20/28 (71%)

Query: 226 STTGQSENVDFVRTYDTVEFLSADTTTT 253 (SEQ ID NO:156)
S Q EN+DFV TYDTV+F+S D TT (SEQ ID NO:157)
Sbjct: 1530 SANNQVENIDFVATYDTVDFVSGDKDTT 1557 (SEQ ID NO:158)

Please amend the paragraph beginning on page 71, line 32 as follows:

The originally-identified partial strain B sequence (ORF38 (SEQ ID NO:8)) shows 95.2% identity over a 165aa overlap with ORF38a (SEQ ID NO:159):

Please amend the paragraph beginning on page 71, line 54 as follows:

The complete strain B sequence (ORF38-1 (SEQ ID NO:10)) and ORF38a (SEQ ID NO:12) show 98.4% identity in 321 aa overlap:

Please amend the paragraph beginning on page 72, line 26 as follows:
ORF38 (SEQ ID NO:160) and lipo (SEQ ID NO:162) show 38% aa identity (SEQ ID NO:161) in 96 aa overlap:

Please amend the paragraph beginning on page 73, line 29 as follows:
The strain B sequence (ORF44 (SEQ ID NO:14)) shows 99.2% identity over a 124aa overlap with ORF44a (SEQ ID NO:16):

Please amend the paragraph beginning on page 73, line 48 as follows:
ORF44 (SEQ ID NO:163) and LecA (SEQ ID NO:165) protein show 45% aa identity (SEQ ID NO:164) in 91 aa overlap:

Please amend the paragraph beginning on page 75, line 50 as follows:
ORF49 (SEQ ID NO:18) shows 86.1% identity over a 173aa overlap with an ORF (ORF49a (SEQ ID NO:166)) from strain A of *N. meningitidis*:

Please amend the paragraph beginning on page 76, line 18 as follows:
ORF49-1 (SEQ ID NO:168) and ORF49a (SEQ ID NO:167) show 83.2% identity in 457 aa overlap:

Please amend the paragraph beginning on page 79, line 58 as follows:
ORF39 (SEQ ID NO:169) shows 100% identity over a 165aa overlap with an ORF (ORF39a (SEQ ID NO:170)) from strain A of *N. meningitidis*:

Please amend the paragraph beginning on page 80, line 23 as follows:

ORF39-1 (SEQ ID NO:28) and ORF39a (SEQ ID NO:30) show 99.4% identity in 710 aa overlap:

Please amend the paragraph beginning on page 82, lines 53-55 as follows:

Query: 680 DKGRIVEAGTQQELLAKPNGYYRYLYDLQN 709 (SEQ ID NO:171)
+KG+IVE G +ELLA PNG Y YL+ LQ+ (SEQ ID NO:172)
Sbjct: 677 EKGQIVEQGKHKELLADPNGLYHYLHQLQS 706 (SEQ ID NO:173)

Please amend the paragraph beginning on page 82, line 59 as follows:

ORF39 (SEQ ID NO:174) and HlyB (SEQ ID NO:176) protein show 71% and 69% amino acid identity (SEQ ID NO:175) in 167 and 55 overlap at the N- and C-terminal regions, respectively:

Please amend the paragraph beginning on page 85, line 19 as follows:

ORF69 (SEQ ID NO:42) shows 96.2% identity over a 78aa overlap with an ORF (ORF69a (SEQ ID NO:44)) from strain A of *N. meningitidis*:

Please amend the paragraph beginning on page 87, line 3 as follows:

ORF77 (SEQ ID NO:46) shows 96.5% identity over a 173aa overlap with an ORF (ORF77a (SEQ ID NO:50)) from strain A of *N. meningitidis*:

Please amend the paragraph beginning on page 87, line 28 as follows:

ORF77-1 (SEQ ID NO:48) and ORF77a (SEQ ID NO:50) show 96.8% identity in 185 aa overlap:

Please amend the paragraph beginning on page 89, line 12 as follows:

ORF112 (SEQ ID NO:52) shows 96.4% identity over a 166aa overlap with an ORF (ORF112a (SEQ ID NO:177)) from strain A of *N. meningitidis*:

Please amend the paragraph beginning on page 90, line 12 as follows:
ORF112a (SEQ ID NO:56) and ORF112-1 (SEQ ID NO:54) show 96.3% identity in 326 aa overlap:

Please amend the paragraph beginning on page 93, line 44 as follows:
ORF114 (SEQ ID NO:58) shows 91.9% identity over a 284aa overlap with an ORF (ORF114a (SEQ ID NO:178)) from strain A of *N. meningitidis*:

Please amend the paragraph beginning on page 96, line 11 as follows:
ORF114-1 (SEQ ID NO:179) and ORF114a (SEQ ID NO:62) show 89.8% identity in 1564 aa overlap

Please amend the paragraph beginning on page 97, line 51 as follows:
ORF114 (SEQ ID NO:180) and pspA (SEQ ID NO:182) protein show 36% aa identity (SEQ ID NO:181) in 302aa overlap:

Please amend the paragraph beginning on page 98, lines 62-64 as follows:

Query: 626 GNI 628 (SEQ ID NO:183)
 GNI (SEQ ID NO:184)
Sbjct: 620 GNI 622 (SEQ ID NO:185)

Please amend the paragraph beginning on page 99, lines 31-33 as follows:

Query: 627 NIVSDGLHAVSA 638 (SEQ ID NO:186)
 + ++A++A (SEQ ID NO:187)
Sbjct: 1413 KSKNSRVNAAA 1424 (SEQ ID NO:188)

Please amend the paragraph beginning on page 100, line 39 as follows:
ORF116 (SEQ ID NO:189) and pspA (SEQ ID NO:191) protein show 38% aa identity
(SEQ ID NO:190) in 502aa overlap:

Please amend the paragraph beginning on page 103, line 12 as follows:
ORF41 (SEQ ID NO:192) shows 92.8% identity over a 279aa overlap with an ORF
(ORF41a (SEQ ID NO:193)) from strain A of *N. meningitidis*:

Please amend the paragraph beginning on page 104, line 40 as follows:
ORF41a (SEQ ID NO:72) and ORF41-1 (SEQ ID NO:70) show 94.8% identity in 595 aa
overlap:

Please amend the paragraph beginning on page 106, line 33 as follows:
ORF51 (SEQ ID NO:74) shows 96.7% identity over a 150aa overlap with an ORF
(ORF51a (SEQ ID NO:194)) from strain A of *N. meningitidis*:

Please amend the paragraph beginning on page 106, line 52 as follows:
ORF51-1 (SEQ ID NO:76) and ORF51a (SEQ ID NO:78) show 99.2% identity in 255 aa
overlap:

Please amend the paragraph beginning on page 108, line 33 as follows:
ORF82 (SEQ ID NO:80) shows 97.1% identity over a 172aa overlap with an ORF
(ORF82a (SEQ ID NO:195)) from strain A of *N. meningitidis*:

Please amend the paragraph beginning on page 109, line 1 as follows:
ORF82a (SEQ ID NO:84) and ORF82-1 (SEQ ID NO:82) show 99.2% identity in 242 aa
overlap:

Please amend the paragraph beginning on page 110, line 31 as follows:
ORF124 (SEQ ID NO:86) shows 87.5% identity over a 152aa overlap with an ORF
(ORF124a (SEQ ID NO:90)) from strain A of *N. meningitidis*:

Please amend the paragraph beginning on page 111, line 1 as follows:
ORF124a (SEQ ID NO:90) and ORF124-1 (SEQ ID NO:88) show 89.5% identity
in 152 aa overlap:

On page 116 after line 6, please insert the following:
-- Sequence Listing--
then insert the 270 pages of the sequence listing.